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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	R. J. Peach, J. R. Naemura, P. S. Linsley and J. Bajorath	
Serial No	:	09/865,321	**Examiner :** Not Yet Known
Filed	:	May 23, 2001	**Group Unit:** Not Yet Known
For	:	SOLUBLE CTLA4 MUTANT MOLECULES AND USES THEREOF	

35 No. Arroyo Parkway
Pasadena, California 91103
July 10, 2001

Honorable Assistant Commissioner for Patents
Washington, D.C. 20231

SIR:

PRELIMINARY AMENDMENT

This communication is being submitted to preliminarily amend the above-identified application.

Please amend the subject application as follows:

In the Specification :

In the description of figures, and in accordance with 37 C.F.R. §§1.121(b)(1)(i) and (ii), on page 4, line 19, please delete the paragraph beginning with "Figures 3A & 3B" and replace it with the following rewritten paragraph:

A1 ~ Figures 3A & 3B depict inhibition of proliferation of purified human T cells by CD80-positive and CD86-positive CHO cells as described in Example 2, infra. ~

Pursuant to 37 C.F.R. §1.121(b)(1)(iii), attached as Exhibit A is a marked up version of the replacement paragraph showing all changes relative to the previous version of the paragraph.

No fee is deemed necessary in connection with the filing of this communication. If any fee is necessary, the Patent Office is authorized to charge the amount of any such fee to Deposit Account No. 50-0306.

Respectfully submitted,

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EXHIBIT A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

There remains a need for improved CTLA4 molecules to provide better pharmaceutical compositions for immune suppression and cancer treatment than previously known soluble forms of CTLA4.

SUMMARY OF INVENTION

Accordingly, the invention provides soluble CTLA4 mutant molecules that bind CD80 and/or CD86. Mutant molecules of the invention include those that can recognize and bind either of CD80, CD86, or both. In some embodiments, mutant molecules bind CD80 and/or CD86 with greater avidity than CTLA4.

One example of a CTLA4 mutant molecule is L104EA29YIg (Figure 7), as described herein. Another example of a CTLA4 mutant molecule is L104EIg (Figure 8), as described herein. L104EA29YIg and L104EIg bind CD80 and CD86 more avidly than CTLA4Ig.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 shows the equilibrium binding analysis of L104EA29YIg, L104EIg, and wild-type CTLA4Ig to CD86Ig.

Figures 2A & 2B illustrate data from FACS assays showing binding of L104EA29YIg, L104EIg, and CTLA4Ig to human CD80- or CD86-transfected CHO cells as described in Example 2, infra.

Figures 3A & 3B depicts inhibition of proliferation of **purified human T cells by** CD80-positive and CD86-positive CHO cells as described in Example 2, infra.

Figures 4A & 4B shows that L104EA29YIg is more effective than CTLA4Ig at inhibiting proliferation of primary and secondary allostimulated T cells as described in Example 2, infra.

Figures 5A-C illustrate that L104EA29YIg is more effective than CTLA4Ig at inhibiting IL-2 (FIG. 5A), IL-4 (FIG. 5B), and γ-interferon (FIG. 5C) cytokine production of allostimulated human T cells as described in Example 2, infra.